Reactions of diphenylketene and methylphenylketene with some *cis*-cyclohexa-3,5-diene-1,2-diol derivatives

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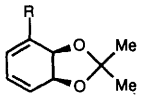
The reaction of the dienes 1–5 with diphenylketene to give the [2 + 2]-adducts 6–10 and the [4 + 2]-adducts 11–15, respectively, has been found to occur by an ionic mechanism involving the zwitterion 16. The reactions of the dienes 2 and 3 with methylphenylketene (and also cyclohexa-1,3-diene with diphenylketene) proceed in a similar fashion. The enol ether 13 was converted into the polyoxygenated cyclohexane derivatives 33, 35 and 38.

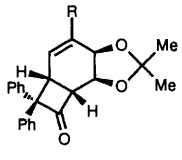
Introduction and background information

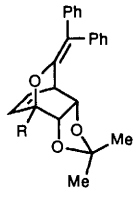
Ketenes generally react with conjugated dienes in a [2+2] fashion to produce cyclobutanones.[1] [4+2] Cycloaddition across the carbon–carbon double bond of a ketene is rare and has only been observed from the reactions of sterically congested diene systems.[2] Woodward and Hoffmann [3] have speculated that the [2+2] pathway preferentially occurs through the initial participation of the low energy $\Pi^*_{C=O}$ orbital of the ketene followed by a concerted $[_\pi 2_s + _\pi 2_a]$ cycloaddition of the two components. More recently, a concerted $[_\pi 2_s(_\pi 2_s + _\pi 2_s)]$ pathway[4] and an ionic pathway[5] have also been proposed.

In contrast, [4+2] cycloaddition across the carbon–oxygen double bond of a ketene has received little attention. Such reactions were thought to only occur in a limited number of cases involving particularly reactive ketene or diene derivatives.[6] However, we have recently reported that a variety of *cis*-cyclohexadiene-diol acetal derivatives **1–5** react with diphenylketene in THF at reflux to afford the [2+2] and [4+2] cycloaddition products **6–10** and **11–15**, respectively.[7]

The fluoro and methyl dienes **1** and **2** were shown to favour the formation of the [4+2] cycloaddition products **11** and **12**, whereas the chloro and bromo dienes **4** and **5** favoured the [2+2] cycloaddition products **9** and **10**; the unsubstituted diene **3** gave almost equimolar quantities of the adducts **8** and **13**.

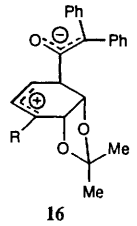






1	R=F	**6**	R=F	**11**
2	R=Me	**7**	R=Me	**12**
3	R=H	**8**	R=H	**13**
4	R=Cl	**9**	R=Cl	**14**
5	R=Br	**10**	R=Br	**15**

The methyl adducts **7/12**, the chloro adducts, **9/14** and the bromo adducts **10/15** readily isomerised in THF or octane solvents at reflux to afford similar product ratios to those obtained from the cycloadditions.‡ In contrast, the unsubstituted adducts **8/13** were stable in THF but readily interconverted in octane to afford, once again, an equimolar mixture of the adducts **8** and **13**. The fluoro[4+2] adduct **11** was stable in both hot THF and boiling octane, but the fluoro-[2+2] adduct **6** was readily converted into the adduct **11** under reflux in these solvents.



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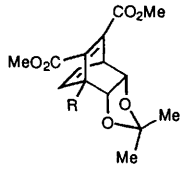
In a recent review, Tidwell proposed that the reaction of *cis*-cyclohexadiene-diol acetals with diphenylketene, and the isomerisation reactions of the resultant adducts, probably occur by an ionic mechanism involving the zwitterionic intermediate **16**.[1]

This paper provides evidence in support of this ionic mechanism. In addition, we show that the reactions of methylphenylketene with the cyclohexadiene-*cis*-diol acetal derivatives **2** and **3**, and the reaction of diphenylketene with cyclohexa-1,3-diene are analogous.

Results and discussion

The dienes **1** and **3** readily afford the adducts **17** and **18** on treatment with dimethyl acetylenedicarboxylate (DMAD).[8] The bromo diene **5** also reacts in a similar manner to give the adduct **19** in high yield.



17 X=F
18 X=H
19 X=Br

Thermolysis of the isolated bromo adducts **10/15** and the fluoro adducts **6/11** in THF at reflux in the presence of an excess of DMAD afforded no 'crossover' products (Table 1).

Trapping reactions performed in octane and DMAD at reflux gave the results summarised in Table 2. The fluoro[4+2] adduct **11** afforded unchanged starting material; the same compound was the only product detected on thermolysis of

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‡ The respective dienes **4** and **5** were also detected (by ^{1}H NMR spectroscopic analysis) in the crude reaction mixtures obtained on thermolysis of the chloro adducts **9/14** and the bromo adducts **10/15** in octane.

Table 1 Thermolysis of some *cis*-cyclohexadiene-diol acetal/diphenylketene adducts in THF with an excess of dimethyl acetylenedicarboxylate

Compound	Time/h	Yield (%) DMAD adduct	[2+2] Adduct	[4+2] Adduct
6 F[2+2]	48	ND	ND	90
11 F[4+2]	48	ND	ND	98
10 Br[2+2]	24	ND	63[a]	11[a]
15 Br[4+2]	24	ND	74[a]	17[a]

[a] Yields determined by high-resolution ^{1}H NMR spectroscopic analysis of the adduct mixture. ND = Not detected.

Table 2 Thermolysis of some *cis*-cyclohexadiene-diol acetal/diphenylketene adducts in octane with an excess of dimethyl acetylenedicarboxylate

Compound	Time/h	Yield (%) DMAD adduct	[2+2] Adduct	[4+2] Adduct
6 F[2+2]	24	ND	ND	NQ
11 F[4+2]	23	ND	ND	97
8 H[2+2]	24	38	37[a]	25[a]
13 H[4+2]	28	40	20[a]	20[a]
10 Br[2+2]	25	53	43	ND
15 Br[4+2]	24	30	24[a]	5[a]

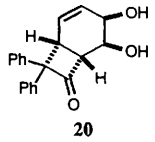
[a] Yields determined by high resolution ^{1}H NMR spectroscopic analysis of the adduct mixture. ND = Not detected. NQ = Not quantified.

the fluoro[2+2] adduct **6** under the same conditions. The unsubstituted adducts **8/13** and the bromo[4+2] adduct **15** all produced mixtures containing the respective [2+2]- and [4+2]-ketene adducts and crossover product, whereas the bromo [2+2] adduct **10** produced only the crossover product **19** (53%) and recovered starting material (43%).

Note that thermolysis of the DMAD adducts **17** and **18** in octane at reflux in the presence of an excess of diphenylketene afforded starting material only.

In a previous communication,[7a] we reported that the optically pure enol ether **13**, when heated in octane for 48 h, produced a mixture of the adducts **8/13**. The [2+2] adduct **8** was optically active, implying that the isomerisation was, at least in part, intramolecular since an entirely intermolecular interconversion between the adducts **8** and **13** would have involved the *meso*-diene **3** resulting in the complete loss of optical activity.

In later work we found that, unlike the adducts **8/13**, the enantiomers of the racemic diol **20** (prepared by the removal of the acetonide unit of the ketone **8**) could be differentiated by chiral shift ^{1}H NMR spectroscopic analysis. This allowed us to quantify more exactly the results of the chirality transfer experiments: hence optically pure enol ether (−)-**13** was heated in octane for 24 h to afford recovered enol ether **13** (27%, 51% optical purity) and the ketone **8** (43%, 58% ee); the enantiomeric excess inherent in the ketone **8** was determined after its subsequent transformation to the diol **20**.



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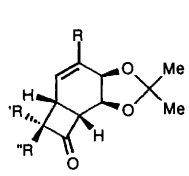
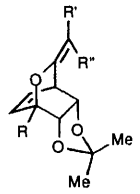
Methylphenylketene (prepared *in situ* from the acyl chloride in THF) reacted with the diene **2** to afford the *endo*-phenyl-[2+2] adduct **21** (53%) and the *Z*-[4+2] adduct **24** (26%). In contrast, the diene **3** produced a 14:2:1 mixture of the *endo*-phenyl-[2+2] adduct **22**, the *Z*-[4+2] adduct **25**, and the *exo*-phenyl-[2+2] adduct **23** (58% overall yield). Trace quantities of the *E*-[4+2] adduct **26** were also detected by high-resolution ^{1}H NMR spectroscopic analysis of the crude reaction mixture, but the compound was not isolated. (Earlier publications report that the adduct **22** is formed exclusively.[9])





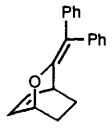
21 R=Me, R'=Ph, R"=Me **24**
22 R=H, R'=Ph, R"=Me **25**
23 R=H, R'=Me, R"=Ph **26**

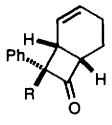
The adducts **21/24**, like their diphenyl analogues **7/12**, underwent slow isomerisation in THF. In octane at reflux, the adducts **21/24** produced equilibrium mixtures favouring the [2+2] adduct **21** (Table 3). The *endo*-phenyl-[2+2] adduct **22** was stable in THF but afforded a 3:1 mixture of the adducts **23** and **25** (4%) in addition to the starting material (87%) after thermolysis in octane for 2 d. The adducts **23** and **25** could not be separated.

Thermolysis of a 1:2 mixture of **23** and **25** for 6 d in THF at reflux afforded a 10:8:4:1 mixture of the adducts **22**, **23**, **25** and **26** from which the *E*-[4+2] adduct **26** was isolated. Thermolysis of the resulting 2:1 mixture of the adducts **23** and **25** in THF at reflux for a further 9 d produced a separable mixture of the [2+2] adducts **22** (15%) and **23** (59%). The *exo*-phenyl-[2+2] adduct **23** was found to be stable in THF and octane at reflux.

Thus, both of the [4+2] isomers (**25** and **26**) are unstable in THF at reflux, and the *exo*-phenyl-[2+2] adduct **23** is, as expected, thermodynamically the more favoured [2+2] isomer.

Cyclohexa-1,3-diene reacted with diphenylketene in THF at reflux over 20 h to produce the [4+2] adduct **27** (14%) in addition to the expected [2+2] adduct **28** (52%).





27 R=Ph **28**
R=Me **29**

Thermolysis of the [4+2] adduct **27** for 5 d in THF at reflux produced a mixture of the adducts **27** and **28** (4:1, 61%), whereas, the [2+2] adduct **28** was stable (Table 4). In octane at reflux, the [4+2] adduct **27** afforded a 5:1 mixture favouring the [2+2] adduct **28** after 2 d, whereas, the [2+2] adduct **28** gave a 13:1 mixture favouring the compound **28**.

Earlier procedures involving the cycloaddition of diphenylketene and cyclohexa-1,3-diene have used sufficiently high temperatures and/or long reaction times such that the [4+2] adduct **27** has isomerised *in situ* and, consequently, has not been observed.[10]

Treatment of cyclohexa-1,3-diene with methylphenylketene in THF at reflux produced the *endo*-phenyl-[2 + 2] adduct **29** exclusively (61%). The adduct **29** is stable in both hot THF and octane.

Table 3 Thermolysis of some *cis*-cyclohexadiene-diol acetal/methylphenylketene adducts in THF and octane solvents at reflux

Adduct	Solvent	Time/d	Yield (%)[a] *endo*-Ph [2+2]	*Z*-[4+2]	*exo*-Ph [2+2]	*E*-[4+2]
21	THF	2	67	11	ND	ND
24	THF	2	32	32	ND	ND
21	Octane	2	68	15	ND	ND
24	Octane	2	57	8	ND	ND
23/25 (2:1)	THF	6	30	12	25	3
23/25 (1:2)	THF	9	15	ND	59	ND
22	THF	6	100	ND	ND	ND
23	THF	2	ND	ND	100	ND
22	Octane	2	87	3	1	ND
23	Octane	2	ND	ND	57	ND

[a] Isolated yields are quoted except compounds **23** and **25** when present together. Ratios of **23/25** in admixture were deterrnined by high resolution ^{1}H NMR spectroscopic analysis. ND = Not detected.

Table 4 Thermolysis of some cyclohexa-1,3-diene/diphenylketene adducts in THF and octane solvents at reflux

Adduct	Solvent	Time/d	Overall yield (%)	Product ratio[a] **27** [2+2]:**29** [4+2]
28 [2+2]	THF	5	61	>20
27 [4+2]	THF	5	74	0.40
28 [2+2]	Octane	2	94	13
27 [4+2]	Octane	2	80	5

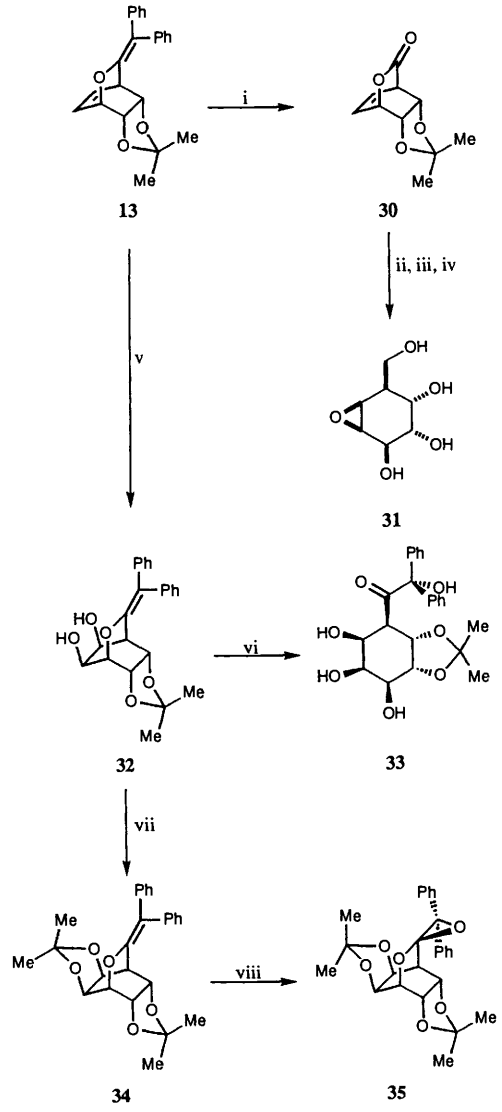
[a] Ratios determined by high resolution ^{1}H NMR spectroscopic analysis of the adduct mixture.

The formation of [4+2] adducts on cycloaddition of diphenylketene to cyclohexadiene-*cis*-diol acetals, and the equilibration of the [2+2] adducts to form more of the same, allows these materials to be used in the synthesis of polyhydroxylated cyclohexane derivatives. We have reported previously the conversion of the [4+2] adduct **13** into the cyclophellitol analogue **31** *via* the synthetically versatile bicyclic lactone **30** (Scheme 1).[7b] More recently we have converted the same adduct into other interesting cyclohexane derivatives. Thus, the optically pure enol ether **13** was readily converted into the *cis*-diol **32** on treatment with a catalytic quantity of osmium tetroxide using potassium ferricyanide as the co-oxidant. The stereochemistry was determined by the subsequent protection of the diol **32** as an acetonide unit; the methyl substituents of the resultant enol ether **34** gave four signals in the ^{1}H and ^{13}C NMR spectra. Treatment of the enol ether **32** with an excess of *m*-CPBA afforded the α-ketol **33** (69%), whereas the enol ether **34**, under the same reaction conditions, gave the spiro acetal **35** (77%).

Presumably, the spiro acetal **35** is stable to further nucleophilic attack due to steric constraints imposed by the substituents flanking the newly formed oxirane ring system, whereas, the spiro acetal **36** is open to intramolecular nucleophilic attack resulting in the α-ketol **33** on subsequent hydrolysis of the intermediate acetal **37** (Scheme 2).

Formation of the spiro acetal **35**, and the inability of the α-ketol **33** to undergo *in situ* Baeyer–Villiger oxidation, add credence to the mechanism previously invoked to account for the formation of the bicyclic lactone **30**.[7a]

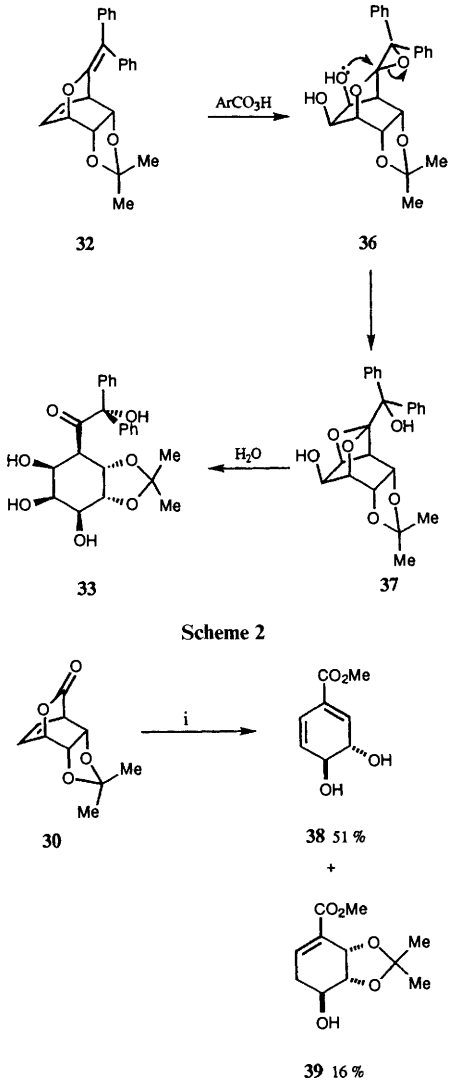
Finally, treatment of the lactone **30** with sodium methoxide in methanol allowed access to the *trans*-cyclohexadiene-diol **38**, the methyl ester of *trans*-3,4-dihydrobenzoic acid, a direct metabolite of chorismic acid.[11]



Scheme 1 *Reagents and conditions:* i, 10 equiv. *m*-CPBA, CH_2Cl_2, pH 7.5 phosphate buffer, 0 °C, 1 h, 55%; ii, $LiAlH_4$, THF, −15 °C, 1 h, 69%; iii, *m*-CPBA, CH_2Cl_2, room temp., 20 h, 85%; iv, Amberlyst 15 (wet) ion-exchange resin, water, room temp., 20 h, 90%; v, cat. OsO_4, $K_3Fe(CN)_6$, K_2CO_3, Bu^{t}OH, water, room temp., 20 h, 61%; vi, 10 equiv. *m*-CPBA, CH_2Cl_2, pH 7.5 phosphate buffer, 0 °C, 2 h, 69%; vii, *p*-TSA, DMP, room temp., 1.5 h, 81%; viii, 10 equiv. *m*-CPBA, CH_2Cl_2, pH 7.5 phosphate buffer, 0 °C, 2 h, 77%

Conclusions

The chirality transfer experiment suggests that the enol ether **13** can be converted into the ketone **8** through a zwitterion of type **16** (or the equivalent diradical). At the temperature of the isomerisation (refluxing octane, bp 128 °C) the intermediate **16** is somewhat unstable, carbon–carbon bond fracture giving diene and ketene: recombination of these components gives



Scheme 2

Scheme 3 *Reagents and conditions:* i, NaOMe, MeOH, CH_2Cl_2, 0 °C, 1.5 h, 67%

racemic enol ether and ketone, diminishing the optical purity of the two components.

These results are broadly in line with the trapping experiments. Pure samples of the enol ether **13** and the isomeric ketone **8** give roughly equal amounts (30 ± 10%) of **8**, **13** and the adduct **18** on reflux with dimethyl acetylenedicarboxylate in octane.

The behaviour of the bromo adducts **10**/**15** follow broadly the same pattern. It is noteworthy that this pair of compounds undergo interconversion in THF with no evidence for intermediate formation of the diene **5**. The ketene adduct **6** gives the [4+2] adduct **11** with no evidence of the formation of the diene **1**. It seems highly likely that the reactions of diphenylketene with the dienes **1**–**5** also proceed by way of a dipolar intermediate **16** rather than through a concerted cycloaddition.

Formation of the [4+2] adducts is not peculiar to the acetals **1**–**5**, cyclohexa-1,3-diene itself reacts with diphenylketene to form a mixture of **27** and **29** in refluxing THF. The [2+2] adduct is thermodynamically the more stable of the pair.

The [4 + 2] adducts are sometimes produced in high yield and the synthetic potential has been illustrated by the facile conversion of **13** into various cyclitols.

Experimental

Unless stated otherwise, all reagents were obtained from commercial suppliers and used without further purification except for *m*-CPBA which was purified by washing with aqueous phosphate buffer (pH 7.5). Light petroleum (bp 40–60 °C) and ethyl acetate were distilled from sodium wire and benzophenone. Dichloromethane was distilled from calcium hydride. Brine refers to saturated aqueous sodium chloride.

Reactions were monitored by TLC on Merck Kieselgel 60 F_{254}, 0.25 mm plates. Plates were visualised using UV light (254 nm) followed by ceric sulfate, dinitrophenylhydrazine, or a dilute aqueous potassium permanganate dip unless stated otherwise. Preparative column chromatography was performed under low pressure using silica gel 60 H Merck (9385). Solvent mixtures are expressed as volume : volume ratios.

250 MHz ^1H and 62.9 MHz ^{13}C NMR spectra were recorded on a Bruker AM 250 spectrometer. 300 MHz ^1H and 76 MHz ^{13}C NMR spectra were recorded on a Bruker AM 300 spectrometer. Chemical shifts (δ) are quoted in ppm downfield to tetramethylsilane and coupling constants (J) are quoted in Hz. IR spectra of KBr discs, chloroform solutions, and neat oils were recorded on a Perkin–Elmer 881 IR spectrophotometer. Optical rotations were measured on a AA-1000 polarimeter operating at the sodium D-line (589.3 nm) and are recorded as 10^{-1} deg cm^2 g^{-1}. Mass spectra were recorded on a Kratos Profile HV-3 spectrometer. Melting points were obtained using an Electrothermal melting point apparatus and are uncorrected.

Ratios of adduct mixtures, after thermolysis and trapping reactions were determined by comparison of the integrals of the distinct ^1H NMR integrals.

Preparation of dimethyl (1*S*,2*S*,6*S*,7*S*)-1-bromo-4,4-dimethyl-3,5-dioxatricyclo[5.2.2.0^{2,6}]undeca-8,10-diene-8,9-dicarboxylate 19

Dimethyl acetylenedicarboxylate (3 cm^3, 0.02 mmol) was added to the diene **5** (0.06 g, 0.25 mmol) in THF (5 cm^3) under dry nitrogen gas. The resultant mixture was boiled under reflux for 24 h after which time the solvent was removed by distillation under reduced pressure. Chromatography of the residue over silica with ethyl acetate–light petroleum (1 : 4) as eluent yielded the diester **19** as a clear colourless oil (0.08 g, 83%), $[\alpha]_D^{28}$ +75.7 (*c* 1.4 in $CHCl_3$); $\nu_{max}(CHCl_3)$/cm^{-1} 3004 (CH_{str}), 2956 (CH_{str}), 1721 ($C{=}O_{str}$), 1264 and 1060; δ_H(300 MHz; $CDCl_3$) 6.41 (1 H, ddd, *J* 8, 2 and 2, 10-H), 6.33 (1 H, m, 11-H), 4.49 (1 H, m, 2-H), 4.40 (2 H, m, 6-H and 7-H), 3.86 (3 H, s, OCH_3), 3.75 (3 H, s, OCH_3), 1.37 (3 H, s, CH_3) and 1.29 (3 H, s, CH_3); δ_C(75.5 MHz; $CDCl_3$) 165.7 (C), 162.5 (C), 149.3 (C), 135.9 (CH), 133.3 (C), 132.2 (CH), 114.5 (C), 84.5 (CH), 79.0 (CH), 60.5 (C), 52.7 (CH_3), 52.5 (CH_3), 41.4 (CH), 25.7 (CH_3) and 25.6 (CH_3) (Found: M$^+$, 372.0195. $C_{15}H_{17}BrO_6$ requires *M*, 372.0209).

Thermolysis of (1*RS*,2*SR*,6*SR*,9*SR*)-7-fluoro-4,4-dimethyl-10,10-diphenyl-3,5-dioxatricyclo[7.2.0.0^{2,6}]undec-7-en-11-one 6 with an excess of dimethyl acetylenedicarboxylate in THF

Dimethyl acetylenedicarboxylate (0.03 cm^3, 0.24 mmol) was added to the ketone **6** (0.01 g, 0.03 mmol) in THF (5 cm^3) under dry nitrogen gas. The resultant mixture was boiled under reflux for 2 d after which time the solvent was removed by distillation under reduced pressure. Chromatography of the residue over silica with ethyl acetate–light petroleum (1 : 15) as eluent yielded the enol ether **11** as a white solid (0.01 g, 90%), ^1H NMR spectroscopic analysis of the crude reaction mixture detected no ketone **6** or diester **17**.

Attempted thermolysis of (1*RS*,2*SR*,6*SR*,7*RS*)-7-fluoro-9-diphenylmethylene-4,4-dimethyl-3,5,8-trioxatricyclo[5.2.2.0^{2,6}]-undec-10-ene 11 with an excess of dimethyl acetylenedicarboxylate in THF

Dimethyl acetylenedicarboxylate (0.13 cm^3, 1.06 mmol) was added to the enol ether **11** (0.05 g, 0.14 mmol) in THF (5 cm^3)

under dry nitrogen gas. The resultant mixture was boiled under reflux for 2 d after which time the solvent was removed by distillation under reduced pressure. Chromatography of the residue over silica with ethyl acetate–light petroleum (1:15) as eluent yielded the enol ether **11** as a white solid (0.05 g, 98%). ^{1}H NMR spectroscopic analysis of the crude reaction mixture detected no ketone **6** or diester **17**.

Thermolysis of (1*R*,2*S*,6*S*,9*S*)-7-bromo-4,4-dimethyl-10,10-diphenyl-3,5-dioxatricyclo[7.2.0.0^{2,6}]undec-7-en-11-one 10 with an excess of dimethyl acetylenedicarboxylate in THF

Dimethyl acetylenedicarboxylate (0.14 cm^3, 1.14 mmol) was added to the ketone **10** (0.05 g, 0.11 mmol) in THF (5 cm^3) under dry nitrogen gas. The resultant mixture was boiled under reflux for 24 h after which time the solvent was removed by distillation under reduced pressure. Chromatography of the residue over silica with ethyl acetate–light petroleum (1:15) as eluent yielded a mixture of the enol ether **15** and the ketone **10** (1:5.5) as a white solid (0.04 g, 74%). ^{1}H NMR spectroscopic analysis of the crude reaction mixture detected no diester **19**.

Thermolysis of (1*R*,2*S*,6*S*,7*R*)-7-bromo-9-diphenylmethylene-4,4-dimethyl-3,5,8-trioxatricyclo[5.2.2.0^{2,6}]undec-10-ene 15 with an excess of dimethyl acetylenedicarboxylate in THF

Dimethyl acetylenedicarboxylate (0.14 cm^3, 1.14 mmol) was added to the enol ether **15** (0.06 g, 0.13 mmol) in THF (5 cm^3) under dry nitrogen gas. The resultant mixture was boiled under reflux for 24 h after which time the solvent was removed by distillation under reduced pressure. Chromatography of the residue over silica with ethyl acetate–light petroleum (1:15) as eluent yielded a mixture of the enol ether **15** and the ketone **10** (1:4.5) as a white solid (0.05 g, 91%). ^{1}H NMR spectroscopic analysis of the crude reaction mixture detected no diester **19**.

Thermolysis of compound 6 with an excess of dimethyl acetylenedicarboxylate in octane

Dimethyl acetylenedicarboxylate (0.14 cm^3, 1.14 mmol) was added to the ketone **6** (0.04 g, 0.12 mmol) in octane (5 cm^3) under dry nitrogen gas. The resultant mixture was boiled under reflux for 24 h after which time the solvent was removed by distillation under reduced pressure to afford an intractable mixture. ^{1}H NMR spectroscopic analysis of the crude reaction mixture detected the enol ether **11** but no ketone **6** or diester **17**.

Attempted thermolysis of compound 11 with an excess of dimethyl acetylenedicarboxylate in octane

Dimethyl acetylenedicarboxylate (0.64 cm^3, 5.2 mmol) was added to the enol ether **11** (0.19 g, 0.52 mmol) in octane (5 cm^3) under dry nitrogen gas. The resultant mixture was boiled under reflux for 23 h after which time the solvent was removed by distillation under reduced pressure. Chromatography of the residue over silica with ethyl acetate–light petroleum (1:15) as eluent yielded the enol ether **11** as a white solid (0.18 g, 97%). ^{1}H NMR spectroscopic analysis of the crude reaction mixture detected no ketone **6** or diester **17**.

Thermolysis of (1*RS*,2*SR*,6*RS*,9*RS*)-4,4-dimethyl-10,10-diphenyl-3,5-dioxatricyclo[7.2.0.0^{2,6}]undec-7-en-11-one 8 with an excess of dimethyl acetylenedicarboxylate in octane

Dimethyl acetylenedicarboxylate (0.14 cm^3, 1.14 mmol) was added to the ketone **8** (0.04 g, 0.14 mmol) in octane (5 cm^3) under dry nitrogen gas. The resultant mixture was boiled under reflux for 24 h after which time the solvent was removed by distillation under reduced pressure. Chromatography of the residue over silica with ethyl acetate–light petroleum (1:15) as eluent yielded a mixture of the enol ether **13** and the ketone **8** (1:1.5) as a white solid (0.02 g, 62%). Later fractions with ethyl acetate–light petroleum (1:4) as eluent yielded the diester **18** as a clear colourless oil (0.01 g, 38%), R_F 0.22 (ethyl acetate in light petroleum, 1:4); $\nu_{max}(CHCl_3)/cm^{-1}$ 3002 (CH_{str}) 1719 ($C{=}O_{str}$), 1264 and 1060; δ_H(250 MHz; $CDCl_3$) 6.38 (2 H, m, 10-H and 11-H), 4.38 (2 H, m, 2-H and 6-H), 4.22 (2 H, m, 1-H and 7-H), 3.78 (6 H, s, 2 × OCH_3), 1.33 (3 H, s, CH_3) and 1.25 (3 H, s, CH_3) (Found: M$^+$, 294.1106. $C_{15}H_{18}O_6$ requires *M*, 294.1103).

Thermolysis of (1*RS*,2*SR*,6*RS*,7*SR*)-9-diphenylmethylene-4,4-dimethyl-3,5,8-trioxatricyclo[5.2.2.0^{2,6}]undec-10-ene 13 with an excess of dimethyl acetylenedicarboxylate in octane

Dimethyl acetylenedicarboxylate (0.2 cm^3, 1.63 mmol) was added to the enol ether **13** (0.05 g, 0.14 mmol) in octane (5 cm^3) under dry nitrogen gas. The resultant mixture was boiled under reflux for 28 h after which time the solvent was removed by distillation under reduced pressure. Chromatography of the residue over silica with ethyl acetate–light petroleum (1:15–1:4) as eluent yielded a mixture of the enol ether **13** and the ketone **8** (1:1) as a white solid (0.02 g, 40%). Later fractions yielded the diester **18** as a clear colourless oil (0.02 g, 40%).

Thermolysis of compound 10 with an excess of dimethyl acetylenedicarboxylate in octane

Dimethyl acetylenedicarboxylate (0.16 cm^3, 1.3 mmol) was added to the ketone **10** (0.05 g, 0.13 mmol) in octane (5 cm^3) under dry nitrogen gas. The resultant mixture was boiled under reflux for 25 h after which time the solvent was removed by distillation under reduced pressure. Chromatography of the residue over silica with ethyl acetate–light petroleum (1:15–1:4) as eluent yielded the ketone **10** as a white solid (0.03 g, 43%). Later fractions yielded the diester **19** as a clear colourless oil (0.02 g, 53%). ^{1}H NMR spectroscopic analysis of the crude reaction mixture detected no enol ether **15**.

Thermolysis of compound 15 with an excess of dimethyl acetylenedicarboxylate in octane

Dimethyl acetylenedicarboxylate (0.14 cm^3, 1.14 mmol) was added to the enol ether **15** (0.05 g, 0.13 mmol) in octane (5 cm^3) under dry nitrogen gas. The resultant mixture was boiled under reflux for 24 h after which time the solvent was removed by distillation under reduced pressure. Chromatography of the residue over silica with ethyl acetate–light petroleum (1:15–1:4) as eluent yielded a mixture of the enol ether **15** and the ketone **10** (1:5) as a white solid (0.02 g, 29%). Later fractions yielded the diester **19** as a clear colourless oil (0.01 g, 30%).

Thermolysis of dimethyl (1*SR*,2*SR*,6*SR*,7*SR*)-1-fluoro-4,4-dimethyl-3,5-dioxatricyclo[5.2.2.0^{2,6}]undec-8,10-diene-8,9-dicarboxylate 17 with an excess of diphenylketene in octane

Diphenylketene (0.20 g, 1.00 mmol) was added to the diester **17** (0.03 g, 0.01 mmol) in octane (10 cm^3) under dry nitrogen gas. The resultant mixture was boiled under reflux for 24 h after which time the solvent was removed by distillation under reduced pressure. Chromatography of the residue over silica with ethyl acetate–light petroleum (1:4) as eluent yielded the diester **17** as a clear colourless oil (0.02 g, 79%). ^{1}H NMR spectroscopic analysis of the crude reaction mixture detected no ketone **6** or enol ether **11**.

Thermolysis of dimethyl (1*RS*,2*RS*,6*SR*,7*SR*)-4,4-dimethyl-3,5-dioxatricyclo[5.2.2.0^{2,6}]undec-8,10-diene-8,9-dicarboxylate 18 with an excess of diphenylketene in octane

Diphenylketene (0.17 g, 0.88 mmol) was added to the diester **18** (0.02 g, 0.07 mmol) in octane (5 cm^3) under dry nitrogen gas. The resultant mixture was boiled under reflux for 24 h after which time the solvent was removed by distillation under reduced pressure. Chromatography of the residue over silica with ethyl acetate–light petroleum (1:4) as eluent yielded the diester **18** as a clear colourless oil (0.01 g, 71%). ^{1}H NMR

spectroscopic analysis of the crude reaction mixture detected no ketone **8** or enol ether **13**.

Preparation of (1*RS*,4*RS*,5*SR*,6*RS*)-4,5-dihydroxy-8,8-diphenylbicyclo[4.2.0]oct-2-en-7-one 20

Toluene-p-sulfonic acid (0.10 g, 0.53 mmol) was added to the ketone **8** (2.82 g, 8.17 mmol) in diethyl ether (200 cm^3) and methanol (100 cm^3) which was then vigorously stirred at room temp. for 5 d. The reaction was quenched with triethylamine (0.5 cm^3) and the solvent removed by distillation under reduced pressure. The residue was diluted with diethyl ether (200 cm^3) and washed with saturated aqueous sodium hydrogen carbonate (2 × 100 cm^3). The aqueous layer was back-washed with diethyl ether (50 cm^3). The combined organic layers were dried ($MgSO_4$) and the solvent was removed by distillation under reduced pressure. The residue was purified by chromatography over silica with ethyl acetate–light petroleum (1 : 1) as eluent to yield the ketone **20** as a white solid (1.54 g, 62%), R_F 0.32 (ethyl acetate in light petroleum, 1 : 1); $\nu_{max}(CHCl_3)/cm^{-1}$ 3340 (OH_{str}), 3011 (CH_{str}), 1771 ($C{=}O_{str}$), 1204 and 1061; δ_H(250 MHz; $CDCl_3$) 7.58–7.11 (10 H, ArH), 5.74 (1 H, m, 3-H), 5.60 (1 H, m, 2-H), 4.29 (1 H, m, 5-H), 4.24 (1 H, m, 4-H), 3.97 (2 H, m, 1-H and 6-H) and 2.94 (2 H, br s, 2 × OH); δ_C(75.5 MHz; $CDCl_3$) 207.5 (CO), 140.3 (C), 139.6 (C), 130.0–126.8 (12 × CH), 77.2 (C), 65.4 (2 × CH), 58.3 (CH) and 34.2 (CH) (Found: M^+, 306.1252. $C_{20}H_{18}O_3$ requires *M*, 306.1256).

Thermolysis of compound 13 in octane

The enol ether (−)-**13** (0.06 g, 0.17 mmol) in dry octane (5 cm^3) was heated at reflux under dry nitrogen gas for 24 h. The solvent was removed by distillation under reduced pressure and the residue purified by chromatography over silica with ethyl acetate–light petroleum (1 : 15) as eluent to yield the enol ether **13** as a white solid (0.02 g, 27%), $[\alpha]_D^{28}$ −32.8 (*c* 0.3 in $CHCl_3$). Later fractions yielded the ketone **8** as a white solid (0.03 g, 43%). Toluene-*p*-sulfonic acid (0.01 g, 0.05 mmol) was added to the ketone **8** (0.16 g, 0.07 mmol) in diethyl ether (2 cm^3) and methanol (1 cm^3) which was then vigorously stirred at room temp. for 6 d. The reaction was quenched with triethylamine (0.5 cm^3) and the solvent removed by distillation under reduced pressure. The residue was purified by chromatography over silica with ethyl acetate–light petroleum (1 : 1) as eluent to yield the ketone **20** as a white solid (0.01 g, 52%). Chiral shift NMR was used to determine the enantiomeric excess (58% ee) of the product using tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]europium(III) as the shift reagent.

Preparation of (1*R*,2*S*,6*S*,7*S*)-9-[(*Z*)-1-phenylethylidene]-4,4,7-trimethyl-3,5,8-trioxatricyclo[5.2.2.0^{2,6}]undec-10-ene 24 and (1*R*,2*S*,6*R*,9*R*,10*S*)-4,4,7,10-tetramethyl-10-phenyl-3,5-dioxatricyclo[7.2.0.0^{2,6}]undec-7-en-11-one 21 in THF

Triethylamine (1.26 cm^3, 9.06 mmol) was added dropwise to 2-phenylpropanoyl chloride (1.52 g, 9.06 mmol) in THF (50 cm^3) with vigorous stirring under dry nitrogen gas. The diene **2** (1.00 g, 6.05 mmol) was then added to the mixture which after being boiled under reflux for 20 h was quenched with water (20 cm^3), adjusted to pH 8 with saturated aqueous sodium hydrogen carbonate and extracted with diethyl ether (3 × 40 cm^3). The combined extracts were washed successively with water (60 cm^3) and brine (60 cm^3), and then dried ($MgSO_4$) after which solvent was removed by distillation under reduced pressure. The products were isolated by chromatography of the residue over silica with ethyl acetate–light petroleum (1 : 15) as eluent to yield the enol ether **24** as a clear colourless oil (0.47 g, 26%), $[\alpha]_D^{26}$ −68.2 (*c* 0.9 in $CHCl_3$), R_F 0.18 (ethyl acetate in light petroleum, 1 : 15); $\nu_{max}(CHCl_3)/cm^{-1}$ 2989 (CH_{str}), 2937 (CH_{str}), 1657 ($C{-}C_{str}$), 1382 and 1070; δ_H(300 MHz; $CDCl_3$) 7.56–7.09 (5 H, ArH), 6.38 (1 H, ddd, *J* 8, 7 and 1, 10-H), 6.41 (1 H, ddd, *J* 8, 1 and 1, 11-H), 4.44 (1 H, ddd, *J* 7, 4 and 1, 2-H), 4.15 (2 H, m, 1-H and 6-H), 2.08 (3 H, s, CH_3), 1.61 (3 H, s, CH_3), 1.38 (3 H, s, CH_3) and 1.32 (3 H, s, CH_3); δ_C(75.5 MHz; $CDCl_3$) 143.4 (C), 140.6 (C), 133.4–125.4 (7 × CH), 110.2 (C), 104.1 (C), 81.0 (CH), 77.0 (C), 75.1 (CH), 39.6 (CH), 25.7 (CH_3), 25.5 (CH_3), 20.9 (CH_3) and 17.6 (CH_3) (Found: M^+, 298.1566. $C_{19}H_{22}O_3$ requires *M*, 298.1569). Later fractions yielded the ketone **21** as a white solid (0.96 g, 53%), mp 85–86 °C (from light petroleum), $[\alpha]_D^{28}$ −150.1 (*c* 1.1 in $CHCl_3$), R_F 0.14 (ethyl acetate in light petroleum, 1 : 15); $\nu_{max}(CHCl_3)/cm^{-1}$ 2829 (CH_{str}), 2930 (CH_{str}), 1771 ($C{=}O_{str}$), 1068 and 1026; δ_H(300 MHz; $CDCl_3$) 7.34–7.16 (5 H, ArH), 5.14 (1 H, m, 8-H), 4.66 (1 H, dd, *J* 6 and 3, 2-H), 4.24 (2 H, m, 1-H and 6-H), 3.03 (1 H, m, 9-H), 1.73 (3 H, s, CH_3), 1.55 (3 H, s, CH_3), 1.38 (3 H, s, CH_3) and 1.33 (3 H, s, CH_3); δ_C(75.5 MHz; $CDCl_3$) 210.0 (CO), 138.9 (C), 134.0 (C), 128.1–126.4 (5 × CH), 122.0 (CH), 108.8 (C), 72.8 (C), 70.3 (CH), 70.2 (CH), 53.2 (CH), 36.1 (CH), 27.8 (CH_3), 26.5 (CH_3), 26.2 (CH_3) and 19.8 (CH_3) (Found: M^+, 298.1575. $C_{19}H_{22}O_3$ requires *M*, 298.1569).

Thermolysis of compound 21 in THF

The ketone **21** (0.05 g, 0.17 mmol) in dry THF (5 cm^3) was heated at reflux under dry nitrogen gas for 2 d. The solvent was removed by distillation under reduced pressure and the residue purified by chromatography over silica with ethyl acetate–light petroleum (1 : 15) as eluent to yield a mixture of the enol ether **24** and the ketone **21** (1 : 6) as a white solid (0.04 g, 78%).

Thermolysis of compound 24 in THF

The enol ether **24** (0.07 g, 0.23 mmol) in dry THF (5 cm^3) was heated at reflux under dry nitrogen gas for 2 d. The solvent was removed by distillation under reduced pressure and the residue purified by chromatography over silica with ethyl acetate–light petroleum (1 : 15) as eluent to yield a mixture of the enol ether **24** and the ketone **21** (1 : 1) as a clear colourless oil (0.04 g, 63%).

Thermolysis of compound 21 in octane

The ketone **21** (0.06 g, 0.21 mmol) in dry octane (5 cm^3) was heated at reflux under dry nitrogen gas for 2 d. The solvent was removed by distillation under reduced pressure and the residue purified by chromatography over silica with ethyl acetate–light petroleum (1 : 15) as eluent to yield a mixture of the enol ether **24** and the ketone **21** (1 : 5) as a white solid (0.05 g, 82%).

Thermolysis of compound 24 in octane

The enol ether **24** (0.05 g, 0.17 mmol) in dry octane (5 cm^3) was heated at reflux under dry nitrogen gas for 2 d. The solvent was removed by distillation under reduced pressure and the residue purified by chromatography over silica with ethyl acetate–light petroleum (1 : 15) as eluent to yield a mixture of the enol ether **24** and the ketone **21** (1 : 7) as a white solid (0.03 g, 65%).

Preparation of (1*RS*,2*SR*,6*RS*,7*SR*)-4,4-dimethyl-9-[(*E*)-1-phenylethylidene]-3,5,8-trioxatricyclo[5.2.2.0^{2,6}]undec-10-ene 26, (1*RS*,2*SR*,6*RS*,7*SR*)-4,4-dimethyl-9-[(*Z*)-1-phenylethylidene]-3,5,8-trioxatricyclo[5.2.2.0^{2,6}]undec-10-ene 25, (1*RS*,2*SR*,6*RS*,9*RS*,10*RS*)-4,4,10-trimethyl-10-phenyl-3,5-dioxatricyclo[7.2.0.0^{2,6}]undec-7-en-11-one 23 and (1*RS*,2*SR*,6*RS*,9*RS*,10*SR*)-4,4,10-trimethyl-10-phenyl-3,5-dioxatricyclo[7.2.0.0^{2,6}]undec-7-en-11-one 22 in THF

Triethylamine (1.00 cm^3, 7.19 mmol) was added dropwise to 2-phenylpropanoyl chloride (1.23 g, 7.32 mmol) in THF (50 cm^3) with vigorous stirring under dry nitrogen gas. The diene **3** (0.51 g, 3.38 mmol) was then added to the mixture which was then boiled under reflux for 3 d, before being quenched with water (20 cm^3), adjusted to pH 8 with saturated aqueous sodium hydrogen carbonate and extracted with diethyl ether (3 × 40 cm^3). The combined extracts were washed successively with water (60 cm^3) and brine (60 cm^3), and then dried ($MgSO_4$) after which time the solvent was removed by distillation under reduced pressure. The products were isolated by chromatogra-

phy of the residue over silica with ethyl acetate–light petroleum (1:15) as eluent to yield an inseparable mixture of the enol ether **25** and the ketone **23** (2:1) as a clear colourless oil (0.10 g, 11%). Later fractions yielded the ketone **22** as a white solid (0.45 g, 47%), mp 123–124 °C (from light petroleum), R_F 0.10 (ethyl acetate in light petroleum, 1:15); $\nu_{max}(CHCl_3)/cm^{-1}$ 2989 (CH_{str}), 2929 (CH_{str}), 1772 ($C{=}O_{str}$) and 1059; δ_H(300 MHz; $CDCl_3$) 7.41–7.19 (5 H, ArH), 5.48 (2 H, m, 7-H and 8-H), 4.67 (1 H, m, 2-H), 4.39 (1 H, m, 6-H), 4.26 (1 H, dd, *J* 9 and 3, 1-H), 3.07 (1 H, m, 9-H), 1.77 (3 H, s, CH_3), 1.41 (3 H, CH_3) and 1.36 (3 H, s, CH_3); δ_C(75.5 MHz; $CDCl_3$) 209.8 (CO), 138.9 (C), 128.3–126.2 (7 × CH), 109.0 (C), 70.2 (C), 69.5 (2 × CH), 52.9 (CH), 35.3 (CH), 28.0 (CH_3), 26.7 (CH_3) and 26.4 (CH_3) (Found: M^+, 284.1420. $C_{18}H_{20}O_3$ requires *M*, 284.1412). The enol ether **26** was also detected as a minor compound by ^1H NMR spectroscopic analysis of the crude reaction mixture.

Thermolysis of a mixture of compound 25 and (1*RS*,2*SR*,6*RS*,9*RS*,10*RS*)-4,4,10-trimethyl-10-phenyl-3,5-dioxatricyclo-[7.2.0.0^{2,6}]undec-7-en-11-one 23 (2:1) in THF

A mixture of the enol ether **25** and the ketone **23** (2:1) (0.10 g, 0.37 mmol) in dry THF (10 cm^3) was heated at reflux under dry nitrogen gas for 6 d. The solvent was removed by distillation under reduced pressure and the residue purified by chromatography over silica with ethyl acetate–light petroleum (1:15) as eluent to yield the enol ether **26** as a white solid (0.003 g, 3%), R_F 0.16 (ethyl acetate in light petroleum, 1:15); $\nu_{max}(CHCl_3)/cm^{-1}$ 2962 (CH_{str}), 2925 (CH_{str}), 1374, 1261 and 1062; δ_H(300 MHz; $CDCl_3$) 7.38–7.16 (5 H, ArH), 7.34 (1 H, m, 11-H), 7.29 (1 H, m, 10-H), 6.00 (1 H, ddd, *J* 6, 4 and 2, 7-H), 5.53 (1 H, ddd, *J* 7, 4 and 1, 6-H), 5.34 (1 H, ddd, *J* 7, 4 and 1, 2-H), 4.92 (1 H, ddd, *J* 6, 4 and 2, 1-H), 1.93 (3 H, s, CH_3), 1.31 (3 H, s, CH_3) and 1.29 (3 H, s, CH_3) (Found: M^+, 284.1404. $C_{18}H_{20}O_3$ requires *M*, 284.1412). Later fractions yielded an inseparable mixture of the enol ether **25** and the ketone **23** (1:2) as a clear colourless oil (0.04 g, 37%) and the ketone **22** as a white solid (0.03 g, 30%).

Thermolysis of a mixture of compounds 25 and 23 (1:2) in THF

A mixture of the enol ether **25** and the ketone **23** (1:2) (0.04 g, 0.14 mmol) in dry THF (10 cm^3) was heated at reflux under dry nitrogen gas for 9 d. The solvent was removed by distillation under reduced pressure and the residue purified by chromatography over silica with ethyl acetate–light petroleum (1:15) as eluent to yield the ketone **23** as a white solid (0.02 g, 59%), mp 118–120 °C (from light petroleum), R_F 0.14 (ethyl acetate in light petroleum, 1:15); $\nu_{max}(CHCl_3)/cm^{-1}$ 3013 (CH_{str}), 2990 (CH_{str}), 1770 ($C{=}O_{str}$) and 1055; δ_H(300 MHz; $CDCl_3$) 7.42–7.25 (5 H, ArH), 5.98 (1 H, m, 7-H), 5.87 (1 H, m, 8-H), 4.64 (1 H, m, 2-H), 4.52 (1 H, m, 6-H), 4.02 (1 H, m, 9-H), 3.41 (1 H, m, 1-H), 1.39 (3 H, s, CH_3), 1.34 (3 H, s, CH_3) and 1.30 (3 H, s, CH_3); δ_C(75.5 MHz; $CDCl_3$) 209.5 (CO), 142.6 (C), 129.2–125.4 (7 × CH), 109.0 (C), 71.7 (C), 69.5 (CH), 69.4 (CH), 54.5 (CH), 33.2 (CH), 28.0 (CH_3), 26.3 (CH_3) and 20.5 (CH_3) (Found: M^+, 284.1411. $C_{18}H_{20}O_3$ requires *M*, 284.1412). Later fractions yielded the ketone **22** as a white solid (0.01 g, 15%).

Attempted thermolysis of compound 22 in THF

The ketone **22** (0.10 g, 0.36 mmol) in dry THF (10 cm^3) was heated at reflux under dry nitrogen gas for 6 d. The solvent was removed by distillation under reduced pressure and the residue purified by chromatography over silica with ethyl acetate–light petroleum (1:15) as eluent to yield the ketone **22** as a white solid (0.10 g, 100%).

Attempted thermolysis of compound 23 in THF

The ketone **23** (0.02 g, 0.06 mmol) in dry THF (5 cm^3) was heated at reflux under dry nitrogen gas for 2 d. The solvent was removed by distillation under reduced pressure and the residue purified by chromatography over silica with ethyl acetate–light petroleum (1:15) as eluent to yield the ketone **23** as a white solid (0.02 g, 100%).

Thermolysis of compound 22 in octane

The ketone **22** (0.10 g, 0.35 mmol) in dry octane (10 cm^3) was heated at reflux under dry nitrogen gas for 2 d. The solvent was removed by distillation under reduced pressure and the residue purified by chromatography over silica with ethyl acetate–light petroleum (1:15) as eluent to yield an inseparable mixture of the enol ether **25** and the ketone **23** (3:1) as a white solid (0.004 g, 4%). Later fractions yielded the ketone **22** as a white solid (0.09 g, 87%). No enol ether **26** was detected.

Attempted thermolysis of compound 23 in octane

The ketone **23** (0.02 g, 0.06 mmol) in dry octane (5 cm^3) was heated at reflux under dry nitrogen gas for 2 d. The solvent was removed by distillation under reduced pressure and the residue purified by chromatography over silica with ethyl acetate–light petroleum (1:15) as eluent to yield the ketone **23** as a white solid (0.01 g, 57%).

Preparation of (1*RS*,4*SR*)-3-diphenylmethylene-2-oxabicyclo-[2.2.2]oct-5-ene 27 and (1*RS*,6*SR*)-8,8-diphenylbicyclo[4.2.0]-oct-2-en-7-one 28 in THF

Diphenylketene (3.11 g, 16 mmol) was added dropwise to cyclohexa-1,3-diene (1.05 g, 13 mmol) in THF (50 cm^3) under dry nitrogen gas. The resultant mixture was boiled under reflux for 20 h, after which it was quenched with water (20 cm^3), adjusted to pH 8 with saturated aqueous sodium hydrogen carbonate and extracted with diethyl ether (3 × 40 cm^3). The combined extracts were washed successively with water (60 cm^3) and brine (60 cm^3), and then dried ($MgSO_4$) after which time the solvent was removed by distillation under reduced pressure. The products were isolated by chromatography of the residue over silica with dichloromethane–light petroleum (1:3) as eluent to yield the enol ether **27** as a white solid (0.50 g, 14%), mp 114–115 °C (from propanone), R_F 0.3 (dichloromethane in light petroleum, 1:3); $\nu_{max}(CHCl_3)/cm^{-1}$ 3007 (CH_{str}), 2945 (CH_{str}), 1635 ($C{-}C_{str}$), 1019 and 974; δ_H(250 MHz; $CDCl_3$) 7.40–7.03 (10 H, ArH), 6.48 (2 H, m, 5-H and 6-H), 5.01 (1 H, ddd, *J* 7, 4 and 2, 1-H), 3.49 (1 H, ddd, *J* 9, 3 and 3, 4-H), 2.22 (1 H, m, 7-H), 1.80 (1 H, m, 8-H), 1.53 (1 H, ddd, *J* 7, 4 and 2, 7-H) and 1.32 (1 H, m, 8-H); δ_C(62.9 MHz; $CDCl_3$) 152.0 (C), 141.8 (C), 140.3 (C), 133.6–125.1 (12 × CH), 110.5 (C), 70.7 (CH), 35.0 (CH), 26.2 (CH_2) and 21.3 (CH_2) (Found: M^+, 274.1369. $C_{20}H_{18}O$ requires *M*, 274.1358). Later fractions yielded the ketone **28** as a white solid (1.85 g, 52%), mp 132–134 °C (from light petroleum), R_F 0.2 (dichloromethane in light petroleum, 1:3); $\nu_{max}(CHCl_3)/cm^{-1}$ 3031 (CH_{str}), 2934 (CH_{str}), 1770 ($C{=}O_{str}$) and 1493; δ_H(250 MHz; $CDCl_3$) 7.52–7.09 (10 H, ArH), 5.80 (1 H, m, 3-H), 5.70 (1 H, m, 2-H), 3.81 (1 H, m, 1-H), 3.70 (1 H, m, 6-H), 2.04 (3 H, m, 2 × 4-H and 5-H) and 1.59 (1 H, m, 5-H) (Found: M^+, 274.1366. $C_{20}H_{18}O$ requires *M*, 274.1358).

Attempted thermolysis of compound 28 in THF

The ketone **28** (0.05 g, 0.2 mmol) in dry THF (5 cm^3) was heated at reflux under dry nitrogen gas for 5 d. The solvent was removed by distillation under reduced pressure and the residue purified by chromatography over silica with ethyl acetate–light petroleum (1:15) as eluent to yield the ketone **28** as a white solid (0.04 g, 61%).

Thermolysis of compound 27 in THF

The enol ether **27** (0.05 g, 0.2 mmol) in dry THF (5 cm^3) was heated at reflux under dry nitrogen gas for 5 d. The solvent was removed by distillation under reduced pressure and the residue purified by chromatography over silica with ethyl

acetate–light petroleum (1:15) as eluent to yield a mixture of the enol ether **27** and the ketone **28** (2.5:1) as a white solid (0.04 g, 74%).

Thermolysis of compound 28 in octane

The ketone **28** (0.05 g, 0.2 mmol) in dry octane (5 cm^3) was heated at reflux under dry nitrogen gas for 2 d. The solvent was removed by distillation under reduced pressure and the residue purified by chromatography over silica with dichloromethane–light petroleum (1:3) as eluent to yield a mixture of the enol ether **27** and the ketone **28** (1:13) as a white solid (0.05 g, 94%).

Thermolysis of compound 27 in octane

The enol ether **27** (0.03 g, 0.1 mmol) in dry octane (5 cm^3) was heated at reflux under dry nitrogen gas for 2 d. The solvent was removed by distillation under reduced pressure and the residue purified by chromatography over silica with dichloromethane–light petroleum (1:3) as eluent to yield a mixture of the enol ether **27** and the ketone **28** (1:5) as a white solid (0.03 g, 80%).

Preparation of (1*RS*,6*SR*,8*RS*)-8-methyl-8-phenylbicyclo-[4.2.0]oct-2-en-7-one 29 in THF

Triethylamine (5 cm^3, 40 mmol) was added dropwise to a stirred solution of 2-phenylpropanoyl chloride (6.30 g, 40 mmol) in dry THF (50 cm^3) under dry nitrogen gas. Cyclohexa-1,3-diene (1.09 g, 10 mmol) was then added to the mixture which was then boiled under reflux for 26 h, quenched with water (20 cm^3), adjusted to pH 8 with saturated aqueous sodium hydrogen carbonate and extracted with diethyl ether (3 × 40 cm^3). The combined extracts were washed successively with water (60 cm^3) and brine (60 cm^3), and then dried ($MgSO_4$). The solvent was removed by distillation under reduced pressure and the residue purified by chromatography over silica with dichloromethane–light petroleum (1:3) as eluent to yield the ketone **29** as a white solid (2.26 g, 61%), mp 65 °C (from light petroleum); $\nu_{max}(CHCl_3)/cm^{-1}$ 3073 (CH_{str}), 2880 (CH_{str}), 1770 ($C{=}O_{str}$) and 1495; δ_H(400 MHz; $CDCl_3$) 7.45–7.13 (5 H, ArH), 5.66 (1 H, m, 3-H), 5.58 (1 H, m, 2-H), 3.85 (1 H, ddd, *J* 9, 6 and 3, 6-H), 2.99 (1 H, m, 1-H), 2.10 (1 H, m, 5-H), 1.93 (2 H, m, 2 × 4-H), 1.73 (3 H, s, CH_3) and 1.57 (1 H, m, 5-H); δ_C(75.5 MHz; $CDCl_3$) 215.3 (CO), 140.4 (C), 128.8–126.4 (7 × CH), 68.6 (C), 52.7 (CH), 37.3 (CH), 27.3 (CH_3), 21.5 (CH_2) and 19.2 (CH_2) (Found: M^+, 212.1205. $C_{15}H_{16}O$ requires *M*, 212.1201).

Attempted thermolysis of compound 29 in THF

The ketone **29** (0.05 g, 0.2 mmol) in dry THF (5 cm^3) was heated at reflux under dry nitrogen gas for 2 d. The solvent was removed by distillation under reduced pressure and the residue purified by chromatography over silica with dichloromethane–light petroleum (1:3) as eluent to yield the ketone **29** as a white solid (0.05 g, 90%).

Attempted thermolysis of 29 in octane

The ketone **29** (0.04 g, 0.2 mmol) in dry octane (5 cm^3) was heated at reflux under dry nitrogen gas for 2 d. The solvent was removed by distillation under reduced pressure and the residue purified by chromatography over silica with dichloromethane–light petroleum (1:3) as eluent to yield the ketone **29** as a white solid (0.03 g, 72%).

Preparation of (1*R*,2*S*,6*S*,7*S*,10*S*,11*S*)-9-diphenylmethylene-4,4,-dimethyl-3,5,8-trioxatricyclo[5.2.2.$0^{2,6}$]undecane-1,11-diol 32

Potassium ferricyanide (0.30 g, 0.91 mmol), potassium carbonate, (0.13 g, 0.92 mmol) and a solution of osmium tetroxide (12 mg cm^{-3} in *tert*-butyl alcohol) (72 mm^3, 0.04 mmol) were successively added to a stirred solution of the enol ether (−)-**13** (0.10 g, 0.25 mmol) in *tert*-butyl alcohol (10 cm^3) and water (10 cm^3). The reaction mixture was stirred for 20 h after which it was quenched with saturated aqueous sodium metabisulfite (10 cm^3) and stirred for a further 1 h. The resultant mixture was extracted with diethyl ether (3 × 20 cm^3) and the combined extracts were washed with brine (20 cm^3) and then dried ($MgSO_4$). The solvent was removed by distillation under reduced pressure and the residue purified by chromatography over silica with ethyl acetate–light petroleum (1:4) as eluent to yield the title compound **32** as a white solid (0.07 g, 61%), mp 163–165 °C (from chloroform in light petroleum, 1:1), $[\alpha]_D^{26}$ +18.5 (*c* 0.7 in $CHCl_3$), R_F 0.05 (ethyl acetate in light petroleum, 1:4); $\nu_{max}(CHCl_3)/cm^{-1}$ 3542 (OH_{str}), 3009 (CH_{str}), 2938 (CH_{str}), 1642 ($C{-}C_{str}$) and 1064; δ_H(400 MHz; $CDCl_3$) 7.42–7.11 (10 H, ArH), 4.51 (2 H, m, 6-H and 7-H), 4.47 (1 H, m, 2-H), 4.35 (1 H, m, 10-H), 4.24 (1 H, dd, *J* 7 and 7, 11-H), 3.28 (1 H, dd, *J* 4 and 3, 1-H), 2.86 (1 H, d, *J* 7, OH), 2.57 (1 H, d, *J* 6, OH), 1.46 (3 H, s, CH_3) and 1.34 (3 H, s, CH_3); δ_C(75.5 MHz; $CDCl_3$) 144.6 (C), 140.0 (C), 138.9 (C), 130.8–126.2 (10 × CH), 119.5 (C), 110.7 (C), 75.8 (CH), 73.2 (CH), 72.9 (CH), 73.4 (CH), 62.0 (CH), 41.6 (CH), 25.6 (CH_3) and 23.9 (CH_3) (Found: M^+, 380.1619. $C_{23}H_{24}O_5$ requires *M*, 380.1624).

Preparation of (1*R*,2*S*,3*S*,4*S*,5*R*,6*S*)-5-[hydroxy(diphenyl)-acetyl]-8,8-dimethyl-7,9-dioxabicyclo[4.3.0]nonane-3,4-diol 33

To a stirred solution of the enol ether **32** (0.18 g, 0.47 mmol) in dichloromethane (4 cm^3) and aqueous pH 7.5 phosphate buffer (0.1 mol dm^{-3}; 4 cm^3) at 0 °C was added *m*-chloroperoxybenzoic acid (0.74 g, 4.71 mmol). The reaction mixture was stirred for 2 h at room temp. and then quenched with a 1:1 mixture of saturated aqueous sodium metabisulfite and aqueous sodium hydrogen carbonate solution (10 cm^3) and diluted with dichloromethane (50 cm^3). The resultant mixture was washed with saturated aqueous sodium hydrogen carbonate (2 × 50 cm^3), dried ($MgSO_4$) and concentrated by removal of the solvent by distillation under reduced pressure. The residue was purified by recrystallisation from chloroform–light petroleum (1:1) to give the title compound **33** as a white solid (0.56 g, 69%), mp 120 °C (decomp.), $[\alpha]_D^{26}$ −55.0 (*c* 1.3 in $CHCl_3$), R_F 0.15 (ethyl acetate in light petroleum, 1:1); $\nu_{max}(CHCl_3)/cm^{-1}$ 3451 (OH_{str}), 3013 (CH_{str}), 2960 (CH_{str}), 1698 ($C{=}O_{str}$) and 1067; δ_H(300 MHz; $CDCl_3/D_2O$) 7.50–7.28 (10 H, ArH), 4.63 (1 H, dd, *J* 9 and 5, 6-H), 4.54 (1 H, dd, *J* 5 and 3, 1-H), 4.16 (1 H, m, 2-H), 3.90 (1 H, m, 4-H), 3.62 (1 H, dd, *J* 4 and 3, 3-H), 3.53 (1 H, dd, *J* 9 and 2, 5-H), 1.50 (3 H, s, CH_3) and 1.36 (3 H, s, CH_3); δ_C(75.5 MHz; $CDCl_3$) 213.3 (CO), 141.7 (C), 140.6 (C), 128.5–127.4 (10 × CH), 109.9 (C), 85.8 (C), 78.9 (CH), 73.9 (CH), 72.2 (CH), 70.8 (CH), 67.8 (CH), 50.6 (CH), 27.7 (CH_3) and 25.7 (CH_3) (Found: M^+, 414.1662. $C_{23}H_{26}O_7$ requires *M*, 414.1679).

Preparation of (2*R*,6*S*,8*S*,12*S*)-14-diphenylmethylene-4,4,10,10-tetramethyl-3,5,9,11,13-pentoxatetracyclo[5.5.2.$0^{2,6}$.$0^{8,12}$]tetradecane 34

Toluene-*p*-sulfonic acid (0.004 g, 0.02 mmol) was added to the enol ether **32** (0.03 g, 0.08 mmol) in 2,2-dimethoxypropane (2 cm^3) and the mixture stirred vigorously for 1.5 h at room temp. The resultant mixture was adjusted to pH 8 with saturated aqueous sodium hydrogen carbonate and then concentrated by removal of the solvent by distillation under reduced pressure. The residue was dissolved in diethyl ether (20 cm^3) and the solution washed successively with saturated aqueous sodium hydrogen carbonate (2 × 20 cm^3) and brine (20 cm^3), dried ($MgSO_4$) and then concentrated by removal of the solvent by distillation under reduced pressure to yield the title compound **34** as a white solid (0.03 g, 81%), mp 82–85 °C (from light petroleum), $[\alpha]_D^{26}$ +21.7 (*c* 0.4 in $CHCl_3$), R_F 0.13 (ethyl acetate in light petroleum, 1:15); $\nu_{max}(CHCl_3)/cm^{-1}$ 3009 (CH_{str}), 2994 (CH_{str}), 1648 ($C{-}C_{str}$), 1384 and 1073; δ_H(300 MHz; $CDCl_3$) 7.45–7.17 (10 H, ArH), 4.56 (5 H, m, 1-H, 2-H, 6-H, 8-H and 12-H), 3.40 (1 H, dd, *J* 4 and 4, 7-H), 1.59 (3 H, s, CH_3), 1.47 (3 H, s, CH_3), 1.38 (3 H, s, CH_3) and 1.33 (3 H, s, CH_3); δ_C(75.5 MHz;

$CDCl_3$) 144.9 (C), 140.5 (C), 139.1 (C), 130.9–125.8 (10 × CH), 117.9 (C), 110.5 (C), 109.2 (C), 72.9 (CH), 72.7 (CH), 72.0 (CH), 71.4 (CH), 70.1 (CH), 39.4 (CH), 26.1 (CH_3), 25.6 (CH_3), 24.5 (CH_3) and 23.6 (CH_3) (Found: M^+, 420.1942. $C_{26}H_{28}O_5$ requires *M*, 420.1937).

Preparation of (2*R*,6*S*,8*S*,12*S*,14*R*)-4,4,10,10-tetramethyl-3′,3′-diphenylspiro{3,5,9,11,13-pentoxatetracyclo[5.5.2.$0^{2,6}$.$0^{8,12}$]-tetradecane-14,2′-oxirane} 35

To a stirred solution of the enol ether **34** (0.02 g, 0.05 mmol) in dichloromethane (1 cm^3) and aqueous pH 7.5 phosphate buffer (0.1 mol dm^{-3}; 1 cm^3) at 0 °C was added *m*-chloroperoxybenzoic acid (0.07 g, 0.46 mmol). The reaction mixture was stirred for 2 h, after which it was quenched with a 1 : 1 mixture of saturated aqueous sodium metabisulfite and aqueous sodium hydrogen carbonate (10 cm^3) and then diluted with dichloromethane (20 cm^3). The resultant mixture was washed with saturated aqueous sodium hydrogen carbonate (2 × 20 cm^3), dried ($MgSO_4$) and then concentrated by removal of the solvent by distillation under reduced pressure. The residue was purified by chromatography over silica using ethyl acetate in light petroleum (1 : 15) as eluent to give the title compound **35** as a white solid (0.02 g, 77%), mp 94–95 °C (from light petroleum), $[\alpha]_D^{26}$ −32.8 (*c* 0.3 in $CHCl_3$), R_F 0.07 (ethyl acetate in light petroleum, 1 : 15); $\nu_{max}(CHCl_3)/cm^{-1}$ 3009 (CH_{str}), 2994 (CH_{str}), 1602 ($C{-}C_{str}$), 1262 and 1069; δ_H(400 MHz; $CDCl_3$) 7.61–7.21 (10 H, ArH), 4.75 (1 H, dd, *J* 8 and 5, 6-H), 4.66 (1 H, dd, *J* 8 and 4, 2-H), 4.56 (1 H, dd, *J* 8 and 4, 8-H), 4.42 (1 H, dd, *J* 8 and 2, 12-H), 4.34 (1 H, dd, *J* 4 and 2, 1-H), 2.59 (1 H, dd, *J* 5 and 4, 7-H), 1.62 (3 H, s, CH_3), 1.45 (3 H, s, CH_3), 1.38 (3 H, s, CH_3) and 1.34 (3 H, s, CH_3); δ_C(100.6 MHz; $CDCl_3$) 138.5 (C), 137.6 (C), 128.1–127.5 (10 × CH), 110.8 (C), 108.8 (C), 89.5 (C), 77.2 (C), 72.9 (CH), 72.5 (CH), 71.6 (CH), 70.1 (2 × CH), 36.6 (CH), 26.0 (CH_3), 25.7 (CH_3), 24.1 (CH_3) and 23.6 (CH_3) (Found: M^+, 436.1874. $C_{26}H_{28}O_6$ requires *M*, 436.1886).

Preparation of methyl (1*RS*,2*SR*,6*SR*)-2-hydroxy-8,8-dimethyl-7,9-dioxabicyclo[4.3.0]non-4-ene-5-carboxylate 39 and (3*SR*,4*SR*)-methyl 3,4-dihydroxycyclohexa-1,5-diene-1-carboxylate 38

Sodium methoxide (0.01 g, 0.16 mmol) was added to the lactone **30** (0.15 g, 0.77 mmol) in dichloromethane (15 cm^3) and dry methanol (15 cm^3) at 0 °C and the resultant mixture stirred for 1.5 h. The mixture was quenched with saturated aqueous ammonium chloride solution (0.5 cm^3) and then concentrated by removal of the solvent by distillation under reduced pressure. The residue was purified by chromatography over silica with ethyl acetate–light petroleum (1 : 1) as eluent to yield the ester **39** as a clear colourless oil (0.03 g, 16%), R_F 0.24 (ethyl acetate in light petroleum, 1 : 1); $\nu_{max}(CDCl_3)/cm^{-1}$ 3597 (OH_{str}), 2993 (CH_{str}), 2938 (CH_{str}), 1717 ($C{=}O_{str}$), 1247 and 1074; δ_H(300 MHz; $CDCl_3$) 7.04 (1 H, dd, *J* 5 and 3, 4-H), 4.97 (1 H, d, *J* 6, 6-H), 4.02 (1 H, dd, *J* 8 and 6, 1-H), 3.90 (1 H, m, 2-H), 3.80 (3 H, s, OCH_3), 2.62 (1 H, ddd, *J* 19, 5 and 5, 3-H), 2.38 (1 H, s, OH), 2.22 (1 H, ddd, *J* 19, 8 and 3, 3-H), 1.47 (3 H, s, CH_3) and 1.44 (3 H, s, CH_3); δ_C(75.5 MHz; $CDCl_3$) 166.0 (CO), 140.6 (CH), 128.7 (C), 109.7 (C), 78.2 (CH), 71.1 (CH), 68.1 (CH), 52.0 (CH_3), 30.9 (CH_2), 28.3 (CH_3) and 26.1 (CH_3) (Found: M^+, 228.0993. $C_{11}H_{16}O_5$ requires *M*, 228.0998). Later fractions yielded the diol **38** as a clear colourless oil (0.07 g, 51%), R_F 0.11 (ethyl acetate in light petroleum, 1 : 1); $\nu_{max}(CHCl_3)/cm^{-1}$ 3596 (OH_{str}), 3025 (CH_{str}), 2955 (CH_{str}), 1720 ($C{=}O_{str}$), 1260 and 1074; δ_H(300 MHz; $CDCl_3$) 6.92 (1 H, m, 2-H), 6.35 (1 H, ddd, *J* 10, 2 and 2, 6-H), 5.98 (1 H, ddd, *J* 10, 2 and 1, 5-H), 4.61 (1 H, m, 3-H), 4.52 (1 H, m, 4-H), 3.79 (3 H, s, OCH_3), 2.30 (1 H, s, OH) and 2.18 (1 H, s, OH); δ_C(75.5 MHz; $CDCl_3$) 165.2 (CO), 139.8 (CH), 131.9 (CH), 128.1 (C), 122.0 (CH), 74.8 (CH), 73.8 (CH) and 52.1 (CH_3) (Found: M^+, 170.0585. $C_8H_{10}O_4$ requires *M*, 170.0579).

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